REMARKS

Status of the Claims

Claims 1 through 3, 7, 8, 15 through 17, 66 through 68 and 78 are pending. Claims 4-6, 9 through 14, 18 through 65, 69 through 77, 79 and 80 are canceled. Claims 1 through 3, 7, 8, 15 through 17, 66 through 68 and 78 stand rejected by the Examiner. Claim 1 has been amended herein by this Amendment to specify that the transplant cell population are human cells in preparation for transplantation. Support for this amendment can be found throughout the specification. No claims have are newly added herein by this Amendment. It is believed that no new matter has been introduced by way of the amendments made herein above.

Claims 5, 6, 9 through 14, 23 through 30, 33 through 41, 44 through 47, 51 through 53, 69 through 76, 79 and 80 stand are withdrawn from consideration by the Examiner. Of these, claims 5, 6, 9 through 14, 23 through 30, 33 through 41, 44 through 47, 51 through 53 and 69 through 74 remain withdrawn from consideration by the Examiner as being drawn to a non-elected invention. Newly presented claims 75, 76, 79 and 80 have been withdrawn by the Examiner as being directed to a non-elected invention. The Examiner asserts that these claims are drawn to *in vivo* administration and treatment with cells and hydrophilic bile acids and therefore independent or distinct from the originally presented and elected invention for prosecution on the merits.

By this Amendment, claims 5, 6, 9 through 14, 23 through 30, 33 through 41, 44 through 47, 51 through 53, 69 through 76, 79 and 80 are cancelled. It is noted that the Examiner considers the additional step of transplantation into a subject as constituting a patentably distinct invention from the current pending claims under examination. Applicants reserve the right to pursue these claims in a continuing application, e.g., one or more divisional applications.

Rejections under 35 U.S.C. §112

Claims 1-4, 7, 8, 15-19, 66-68, 77 and 78 have been rejected by the Examiner under 35 U.S.C. §112, Second Paragraph, for being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner rejected claim 1 as indefinite by reciting "dopamine neurons or precursors thereof" as lacking a clear definition. Applicant(s) hereby respectfully traverse(s) this rejection for the following reason(s) as applied to the pending claims.

The Examiner argues that the meaning and characterization of "dopamine neurons" is unclear, as well as "differentiated dopamine neurons" and "precursors thereof." To start with, the Examiner is referred to the Background section of the instant application, which explains that the area of the brain referred to as the "substantia nigra" produces dopamine. A neuron is a nerve cell, and nerve cells are well known as being present in brain tissue and the central nervous system (CNS). Well over a dozen journal articles are cited (and incorporated by reference into the application) in the Background section alone which contain discussions of dopamine neurons. Applicants submit, therefore, that the meaning and characterization of "dopamine neurons" is both established and well-understood by those skilled in the art.

As to the Examiner's concern regarding "differentiated" and "precursors," similarly the meaning and characterization of these terms are established and readily understood to cell biologists, for example. "Differentiation" within the context of cell development refers to a change from simple to complex forms so that the cells become specialized for a particular function. The term is applicable to all cells. Likewise, "precursors" in cell development refers to stem cells that have developed to the stage where they are committed to forming a particular kind of cell. "Mesencephalon" is the midbrain. A "neuron" again is a type of cell – a nerve cell. Neurons and nerve cells are subject to being described within the context of the established and applicable cell development terminology and vocabulary.

The Examiner is seeking an exact phraseology match between claim terminology and terminology as it may appear in the specification. The failure to provide explicit antecedent

basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. MPEP §2173.05(e) (6th Ed. Rev.1, Sept. 1995); Ex parte Porter, 25 U.S.P.Q.2d 1144, 1146 (BPAI 1992); In re Moore, 439 F.2d. 1232, 1235, 169 U.S.P.Q. 236, 238 (CCPA 1971). It is submitted by Applicant that the claimed terms objected to by the Examiner do not require explicit expanded definitions or expanded explanations further than the guidance provided in the specification.

The Examiner's concerns have thus been addressed, and the claims are fully compliant with the requirements of 35 U.S.C. §112, second paragraph. This rejection should, therefore, be withdrawn by the Examiner.

Rejections under 35 U.S.C. §102

Claims 1-4, 7, 8, 15-17, 66, 67, 77 and 78 have been rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Rodrigues et al. J. Neurochem., 75 pp.2368-79 (2000). Applicant(s) hereby respectfully traverse(s) this rejection for the following reason(s) as it apples to the pending claims.

The Examiner has asserted that the alleged lack of clarity for the terminology "dopamine neurons and precusors thereof" provides license to broadly apply the Rodrigues reference under the guise of grounds for anticipation of the claimed invention. Applicants have addressed and overcome the Examiner's concerns regarding the language that the Examiner had viewed as lacking definition. Applicants repeat the previous position in the remarks in the Response dated September 18, 2008 on page 12. The Rodrigues reference does not disclose a method pertaining to cells of a human transplantation cell population which are dopamine neurons or precursors thereof as required by the claims.

Because Rodrigues as a single reference does not teach each and every claim element as required for a proper rejection on anticipation grounds, it cannot be said that the claimed

invention is anticipated by Rodrigues. Given the above, the claims as amended are not anticipated by the Rodrigues reference within the proper meaning of 35 U.S.C. §102. This rejection should, therefore, be withdrawn.

Claims 1-4, 7, 8, 15-17, 66, 67, 77 and 78 have been rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Silva et al., J. Hepatol., 34, pp.402-408 (2001). Applicant(s) hereby respectfully traverse(s) this rejection for the following reason(s) as applied to the pending claims.

The Examiner has asserted that the alleged lack of clarity for the terminology "dopamine neurons and precursors thereof" provides license to broadly apply the Silva reference under the guise of grounds for anticipation of the claimed invention. Applicants have addressed and overcome the Examiner's concerns regarding the language that the Examiner had viewed as lacking definition. Applicants repeat the previous position in the remarks in the Response dated September 18, 2008 on page 12. The Silva reference does not disclose a method of promoting cell viability pertaining to cells of a human transplantation cell population which are dopamine neurons or precursors thereof as required by the claims.

Because the Silva reference as a single reference does not teach each and every claim element as required for a proper rejection on anticipation grounds, it cannot be said that the claimed invention is anticipated by the Silva reference. Given the above, the claims are not anticipated by the Silva reference within the proper meaning of 35 U.S.C. §102. This rejection should, therefore, be withdrawn.

Claims 1-4, 7, 8, 15-17, 66, 67, 77 and 78 have been rejected by the Examiner under 35 U.S.C. §102(b) as being anticipated by Duan, Soc. Neurosci. Abst., 29, p.1245 (2001) or Duan et al., Cell Transplantation, 11, pp.195-205 (2002) . Applicant(s) hereby respectfully traverse(s) this rejection for the following reason(s) as applied to the pending claims.

The Examiner argues that the Duan references teach *in vitro* treatment of dopamine neuron cells in rats. The claimed invention has been amended to specify that the transplantation

cell population is composed of human cells. The Duan abstract reference contains no teaching of *in vitro* treatment or preparation of ***human*** dopamine neurons.

Furthermore, the abstract is absent a teaching as to a promoting viability of a *transplant* cell population. A proper rejection under 35 U.S.C. §102 requires that each and every claim element be present in a single reference. This reference does not contain each and every element required by Applicants' claims. Therefore, it cannot be said that the claimed invention is anticipated by Duan abstract.

Duan et al. Cell Transplantation discusses that dopamine neuron transplantation in humans is currently being investigated. The study described in the article, however, pertains to treating rat cells with TUDCA for transplantation into rats. Again, this reference fails to expressly teach TUDCA treatment of ***human*** cells for ***transplantation*** into humans. This reference does not contain each and every element required by Applicants' claims. Therefore, it cannot be said that the claimed invention is anticipated by Duan abstract.

Because the Duan abstract and Duan et al. Cell Transplantation individually as single references do not teach each and every claim element as required for a proper rejection on anticipation grounds, it cannot be said that the claimed invention is anticipated by these references. Given the above, the claims are not anticipated by the Duan, Soc. Neurosci. Abst., 29, p.1245 (2001) or Duan et al., Cell Transplantation, 11, pp.195-205 (2002) references within the proper meaning of 35 U.S.C. §102. These rejections should, therefore, be withdrawn.

Rejections under 35 U.S.C. §103(a)

Claims 1-4, 7, 8, 15-17, 66-68, 77 and 78 have been rejected by the Examiner under 35 U.S.C. §103(a) as being unpatentable over Falasca et al., Transplantation, 71 (9), pp. 195-205 (May 2001); Duan et al., Cell Transplantation, 11, pp.195-205 (2002); Rodrigues et al., J. Neurochem., 75 pp.2368-79 (2000); Silva et al., J. Hepatol., 34, pp.402-408 (2001); and Duan,

Soc. Neurosci. Abstracts, 29, p.1245 (2001). Applicant(s) hereby respectfully traverse(s) this rejection for the following reason(s) as applied to the pending claims.

The Examiner appears to believe that the alleged lack of clarity for the terminology "dopamine neurons and precursors thereof" provides license to broadly apply the Falasca, Rodriquez and Silva references under the guise of grounds for obviousness of the claimed invention. Applicants have addressed and overcome the Examiner's concerns regarding the language that the Examiner had viewed as lacking definition. Applicants repeat the previous position in the remarks in the Response dated September 18, 2008 on page 12. None of the teachings of the Falasca, Rodriguez and Silva references expressly disclose a method of promoting viability pertaining to cells of a human transplantation cell population which are *human* dopamine neurons or precursors thereof as required by the claims.

Falasca pertains to treatment of human liver cells with TUDCA at harvesting and cold storage stage. Liver cells are fundamentally different in morphology, function and biology from dopamine neurons. One of ordinary skill in the cellular biology art would not have viewed the content of Falasca and readily contemplated that a study of storage protective effects of TUDCA on liver cells would fairly indicate success as to dopamine neuron cell transplantation and neuron cellular viability in humans.

The Examiner is correct in stating that the content of Rodrigues and Silva pertain to *rat* cells. Again, Applicants' claimed invention pertains to a method comprising the *in vitro* treatment of human dopamine neuron cells or precursors thereof with a bile salt (e.g., TUDCA) and thus preparing the cell population with enhanced viability for transplantation into a subject. Rodrigues uses neuronal cells RNB33. Silva discusses bilirubin toxicity and bilirubin-induced cell death of hepatic cells and preventing apoptosis using UDCA. No mention of cell transplantation is seen in Silva. No extension of the study or its conclusion toward dopamine neuronal cells in preparation for transplantation is seen either.

Neither Rodrigues nor Silva explicitly mention human dopamine neurons – and nor would they when describing experiments and studies that pertain rat neurons. Rodrigues teaches TUDCA may enhance neuron cell survival, but is absent a teaching or suggestion of a method for promoting viability of human dopamine neuronal cells in preparation for transplantation as claimed by Applicants.

In combination, Falasca, Silva and Rodrigues still have an absence of content that would leave the Examiner to fabricate a bridge to fill gaps in teachings between the references and the claimed invention. Further, these gaps are substantive – and certainly beyond a minimal extent suitable to support a *prima facie* case of obviousness.

The shortcomings of the Duan, Soc. Neurosci. Abstracts, 29, p.1245 (2001); and Duan et al., Cell Transplantation, 11, pp.195-205 (2002) are discussed by Applicants in the above response to the rejection under 35 U.S.C. §102 and are likewise applicable here and repeated herein. The Duan abstract reference contains no teaching of *in vitro* treatment or preparation of *human* dopamine neurons. Furthermore, the abstract is absent a teaching as to promoting viability of a *transplant* cell population. Duan et al. Cell Transplantation mentions that dopamine neuron transplantation in humans is currently being investigated. The study described in the article, however, pertains to treating rat cells with TUDCA for transplantation into rats. Again, this reference fails to expressly teach TUDCA treatment of *human* cells for *transplantation* into humans.

The Examiner applied an inappropriate level of hindsight to piece these teachings together in an attempt to represent that one of ordinary skill in the art would view them and arrive at the claimed invention. Further, the Examiner overreaches "field of endeavor" in attempting to unite all of the references into a shared context. Applicants do not place the content of all of the references cited and applied in this rejection to be the "same" field of endeavor. At best, combining the teachings of some of the references would arrive at *in vitro* treatment of rat neurons with bile salts. This falls short of fairly teaching or suggesting the

claimed invention and its required human dopamine neuronal cells in preparation for transplantation, among other claim elements.

The Examiner has failed to present a combination of references that adequately support a *prima facie* case of obviousness against the claimed invention. None of the above references, taken individually or in combination, can be said to fairly teach or suggest the invention as claimed by Applicant. Furthermore, it is not understood how given the above cited references one of ordinary skill in the art would have been motivated to combine the teachings to arrive at the claimed invention.

Given the above, the claims are not unpatentable as being obvious in view of the above reference(s) within the proper meaning of 35 U.S.C. §103. This rejection should, therefore, be withdrawn.

Conclusion:

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested. The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

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